



App No. 087700,737
Title: "Humanized Immunoglobulin ..."
Inventors: Paul D. Ponnath, et al.

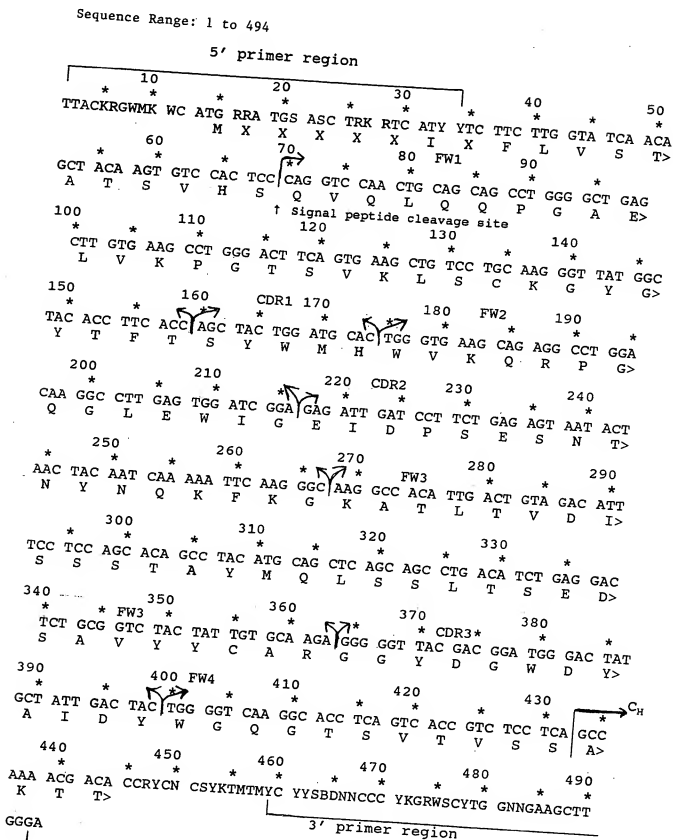


FIG. 1



Title: Humanized Immunoglobulin ...
Inventors: Paul D. Ponath, et al.

Sequence Range: 1 to 428

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      10      20      30      40      50
TTACTTGACG ACTCGGG ATG GGA TGG AGC TAT ATC ATC TTC TTC TTG GTA TCA
      *      *      *      *      *
      60      70      80      90     100
ACA GCT ACA AGT GTC CAC TCC CAG GTC CAA CTG CAG CAG CCT GGG GCT
T   A   T   S   V   H   S   Q   V   Q   L   Q   Q   P   G   A>
      *      *      *      *      *
     110     120     130     140
GAG CTT GTG AAG CCT GGG ACT TCA GTG AAG CTG TCC TGC AAG GGT TAT
E   L   V   K   P   G   T   S   V   K   L   S   C   K   G   Y>
      *      *      *      *      *
    150     160     170     180     190
GGC TAC ACC TTC ACC AGC TAC TGG ATG CAC TGG GTG AAG CAG AGG CCT
G   Y   T   F   T   S   Y   W   M   H   W   V   K   Q   R   P>
      *      *      *      *      *
    200     210     220     230     240
GGA CAA GGC CTT GAG TGG ATC GGA GAG ATT GAT CCT TCT GAG AGT AAT
G   Q   G   L   E   W   I   G   E   I   D   P   S   E   S   N>
      *      *      *      *      *
    250     260     270     280     290
ACT AAC TAC AAT CAA AAA TTC AAG GGC AAG GCC ACA TTG ACT GTA GAC
T   N   Y   N   Q   K   F   K   G   K   A   T   L   T   V   D>
      *      *      *      *      *
    300     310     320     330     340
ATT TCC TCC AGC ACA GCC TAC ATG CAG CTC AGC AGC CTG ACA TCT GAG
I   S   S   S   T   A   Y   M   Q   L   S   S   L   T   S   E>
      *      *      *      *      *
    350     360     370     380
GAC TCT GCG GTC TAC TAT TGT GCA AGA GGG GGT TAC GAC GGA TGG GAC
D   S   A   V   Y   Y   C   A   R   G   G   Y   D   G   W   D>
      *      *      *      *      *
    390     400     410     420
TAT GCT ATT GAC TAC TGG GGT CAA GGC ACA TCA GTC ACC
Y   A   I   D   Y   W   G   Q   G   T   S   V   T>

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FIG. 2



App No.: 08/700,737
Title: "Humanized Immunoglobulin ..."
Inventors: Paul D. Poth, et al.

Sequence Range: 1 to 535

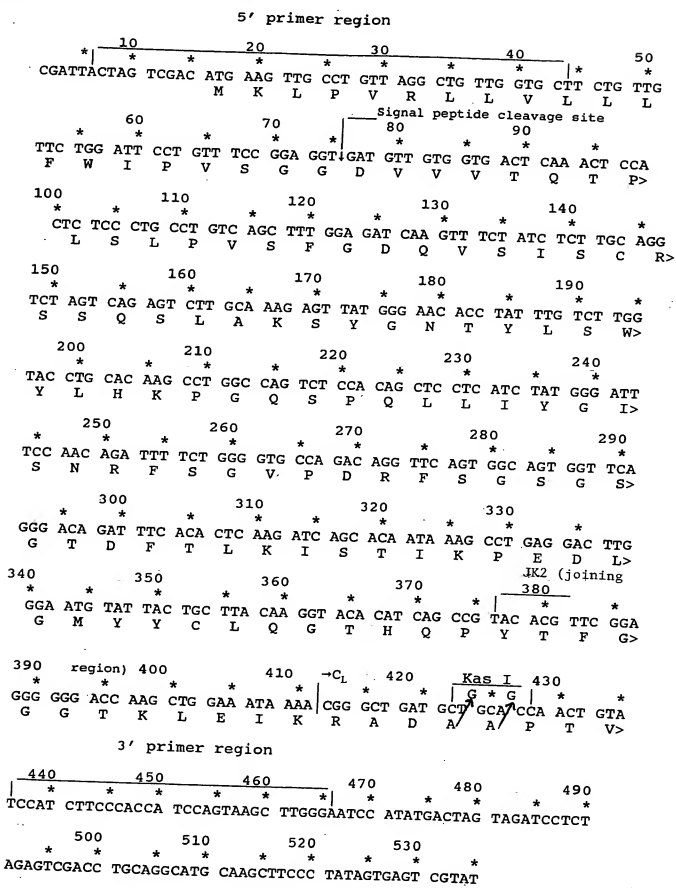


FIG. 3



App No: 05/700,757
Title: Humanized Immunoglobulin ...
Inventors: Paul D. Ponath, *et al.*

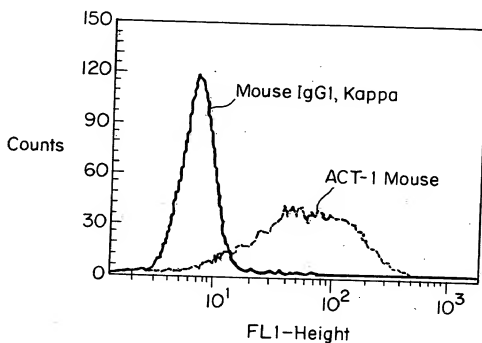


FIG. 4A

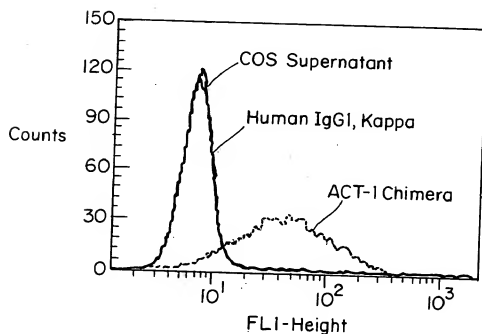


FIG. 4B



Percent similarity: 82.143 Percent Identity: 71.429

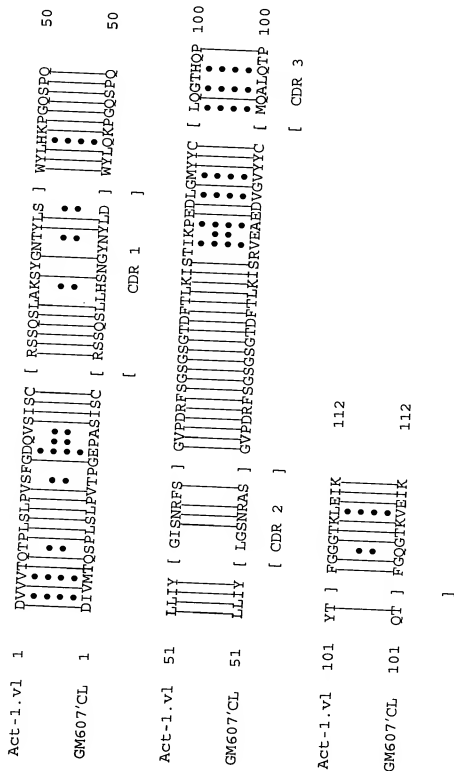


FIG. 5



App. No.: 08/700,737
 Title: "Humanized Immunoglobulin ..."
 Inventors: Paul D. Ponath, et al.

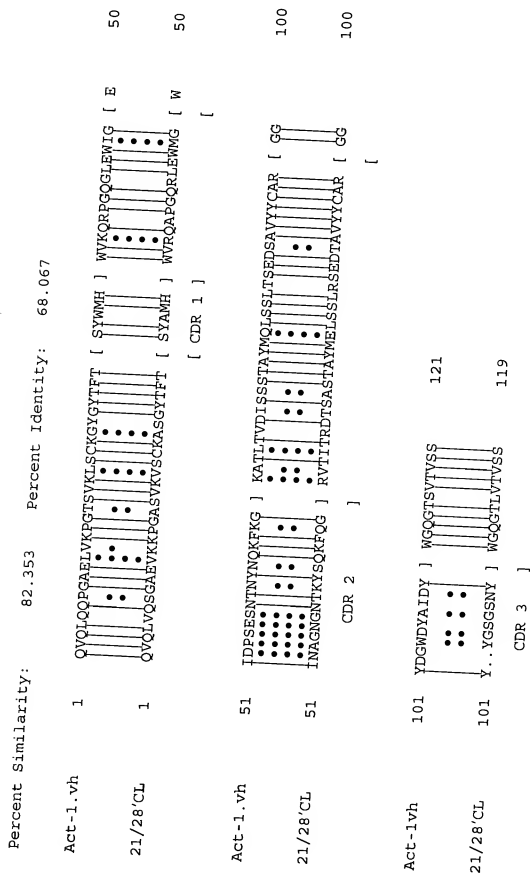


FIG. 6



App No.: 08/700,737
Title: "Humanized Immunoglobulin"
Inventors: Paul D: Ponath, et al.

1 ATGAAGTTGCCTGTTAGGCTGTTGGTGCTTCTGTTGTTCTGGATTCTGTTCCGGAGGT 60
TACTTCAACGGACAATCCGACACCAACGAAGACAACAAGACCTAAGGACAAGGCCTCCA
[M K L P V R L L V L L L F W I P V S G G]
Signal Peptide
61 GATGTTGTGGTGACTCAAACCTCCACTCTCCCTGCCTGTGACGTTGGAGATCAAGTTTCT 120
CTACACACCACTGAGTTTGAGGTGAGAGGGGACGACAGTCGAAACCTCTAGTTCAAAGA
[D V V V T Q T P L S L P V S F G D Q V S]
Framework 1
121 ATCTCTTGCAAGTCTAGTCAGACTCTTGCAAAGAGTTATGGGAACACCTATTGTTCTTGG 180
TAGAGAACGTCACAGATCAGTCTCAGAACGTTTCTCAATACCTTGTGGATAAACAGAAC
I S C][R S S Q S L A K S Y G N T Y L S][W
CDR 1
181 TACCTGCACAAGCCTGGCCAGTCTCCACAGCTCCTCATCTATGGGATTCCAACAGATTT 240
ATGGACGTGTTCCGACCGGTGAGAGGTGTCGAGGAGTAGATACCCCTAAAGGTTGTCTAAA
Y L H K P G Q S P Q L L I Y][G I S N R F
Framework 2
241 TCTGGGGTGCCAGACAGGTTTCAGTGGCAGTGGTTCAGGGACAGATTTCACACTCAAGATC 300
AGACCCACGGTCTGTCCAAGTCACCGTCACCAAGTCCCTGTCTAAAGTGTGAGTTCTAG
S][G V P D R F S G S G S G T D F T L K I
Framework 3
301 AGCACAATAAAGCCTGAGGACTTGGGAATGTATTACTGCTTACAAGGTACACATCAGCCG 360
TCGTGTTATTTCGGACTCTGTAACCCCTTACATAATGACGAATGTTCCATGTGTAGTCGGC
S T I K P E D L G M Y Y C][L Q G T H Q P
CDR 3
361 TACACGTTCCGAGGGGGGACCAAGCTGGAATAAAA 396
ATGTGCAAGCCTCCCCCTGGTTCGACCTTTATTTT
Y T][F G G G T K L E I K]
Framework 4

FIG. 7



1 GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGAGAGCCGGCCTCC 60
 CTATAACACTACTGAGTCAGAGGTGAGAGGGACGGGCAGTGGGGACCTCTCGGCCGGAGG
 [D I V M T Q S P L S L P V T P G E P A S

Framework 1

61 ATTCCTGCGAGGTCTAGTCAGAGCCTCCTCCATAGTAATGGATCAAACCTATTGGATTGG 120
 TAGAGGACGTCCAGATCAGTCTCGGAGGAGGTATCATTACCTAGTTTGATAAACCTAACCC
 I S C][R S S Q S L L H S N G Y N Y L D][W

CDR 1

121 TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCTGATCTATTGGGTTCTAATCGGGCC 180
 ATGGACGTCTTCGGTCCCGTCAGAGGTGTCGAGGACTAGATAAACCCCAAGATTAGCCCGG
 Y L Q K P G Q S P Q L L I Y][L G S N R A

Framework 2

CDR 2

181 TCCGGGGTCCCTGACAGGTTCACTGGCAGTGGATCAGGCACAGATTTTACACTGAAATC 240
 AGGCCCCAGGACTGTCCAAGTCACCGTCACCTAGTCCGTGTCTAAATGTGTCTTTTAG
 S][G V P D R F S G S G S G T D F T L K I

Framework 3

241 AGCAGAGTGGAGGCTGAGGATGTTGGGGTTTATTACTGCATGCAAGCTCTACCAACTCCT 300
 TCGTCTCACCTCCGACTCCTACAACCCCAAATAATGACGTACGTTTCGAGATGGTTGAGGA
 S R V E A E D V G V Y Y C][M Q A L Q T P

CDR 3

301 CAGACGTTCCGCCAAGGGACCAAGTGGAAATCAAA 336
 GTCTGCAAGCCGGTTCCTGGTTCCACCTTTAGTTT
 Q T][F G Q G T K V E I K

Framework 4

FIG. 8

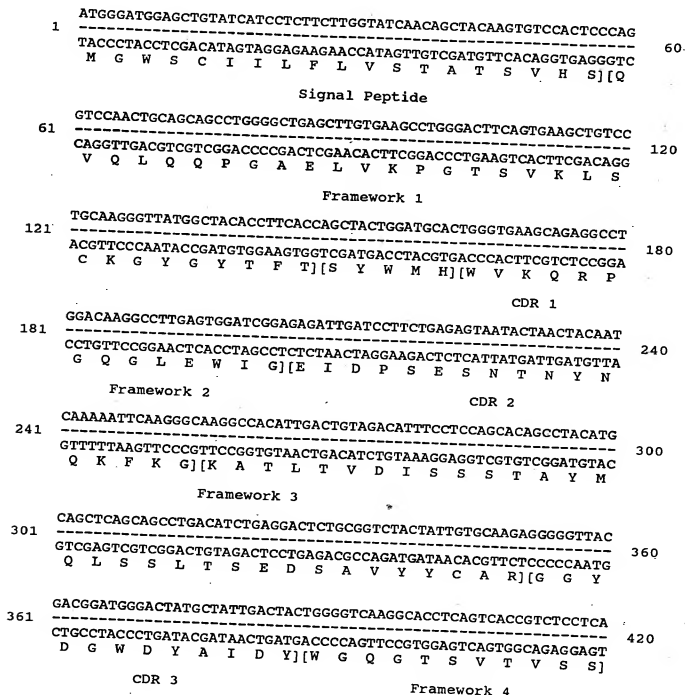


FIG. 9



1 ATGGAGTTTGGGCTGAGCTGGCTTTTCTGTGGCTATTTTAAAAGGTGTCCAGTGTCA

 TACCTCAAACCCGACTCGACCGAAAAAGAACCCGATAAAATTTCCACAGGTACAGT
 [M E F G L S W L F L V A I L K G V Q C][Q] 60

Signal peptide

61 GTGCAGCTTGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCTCAGTGAAGTTTCC

 CACGTGCAACACGTGACACCCGACTCCACTTCTTCGGACCCCGAGTCACTTCCAAAGG
 V Q L V Q S G A E V K K P G A S V K V S 120

Framework 1

121 TGCAAGGCTTCTGGATACACCTTCACTAGCTATGCTATGCATTGGGTGCGCCAGGCCCCC

 ACGTTCCGAAGACCTATGTGGAAGTATCGATACGATACGTAACCCACGCGTCCGGGG
 C K A S G Y T F T][S Y A M H][W V R Q A P 180

CDR 1

181 GGACAAAGGCTTGAGTGGATGGGATGGATCAACGCTGGCAATGTGAACAAAAATATTCA

 CCTGTTTCCGAACCTACCTACCTACCTAGTTGCGACCGTTACCATTTGTGTTTATAAGT
 G Q R L E W M G][W I N A G N G N T K Y S 240

Framework 2

CDR 2

241 CAGAAGTTCAGGGCAGAGTCACCATTAACAGGGACACATCCGCGAGCACAGCCTACATG

 GTCTTCAAGTCCCGTCTCAGTGGTAATGGTCCCTGTGTAGGCGCTCGTGTGGATGTAC
 Q K F Q G][R V T I T R D T S A S T A Y M 300

301 GAGCTGAGCAGCCTGAGATCTGAAGACACGGCTGTGTATTACTGTGCGAGAGGAGTTAC

 CTCGACTCGTCGACTCTAGACTTCTGTGCCGACACATAATGACACGCTCTCCTCCAATG
 E L S S L R S E D T A V Y Y C A R][G G Y 360

Framework 3

361 TATGTTTCGGGGAGCAACTACTGGGGCCAGGGAACCCCTGGTCACCGTCTCCTCA

 ATACCAAGCCCTCGTTGATGACCCCGGTCCCTTGGGACCAAGTGGCAGAGGAGT
 Y G S G S N Y][W G Q G T L V T V S S] 414

CDR 3

Framework 4

FIG. 10



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      10      20      30      40
    *   *   *   *   *   *   *   *
  ATG AAA TGC ACC TGG GTC ATT CTC TTC TTG GTA TCA ACA GCT ACA AGT
  M   K   C   T   W   V   I   L   F   L   V   S   T   A   T   S>

      50      60      70      80      90
    *   *   *   *   *   *   *   *
  GTC CAC TCC CAG GTC CAA CTA GTG CAG TCT GGG GCT GAG GTT AAG AAG
  V   H   S   Q   V   Q   L   V   Q   S   G   A   E   V   K   K>

      100     110     120     130     140
    *   *   *   *   *   *   *   *
  CCT GGG GCT TCA GTG AAG GTG TCC TGC AAG GGT TCT GGC TAC ACC TTC
  P   G   A   S   V   K   V   S   C   K   G   S   G   Y   T   F>

      150     160     170     180     190
    *   *   *   *   *   *   *   *
  ACC AGC TAC TGG ATG CAT TGG GTG AGG CAG GCG CCT GGC CAA CGT CTA
  T   S   Y   W   M   H   W   V   R   Q   A   P   G   Q   R   L>

      200     210     220     230     240
    *   *   *   *   *   *   *   *
  GAG TGG ATC GGA GAG ATT GAT CCT TCT GAG AGT AAT ACT AAC TAC AAT
  E   W   I   G   E   I   D   P   S   E   S   N   T   N   Y   N>

      250     260     270     280     290
    *   *   *   *   *   *   *   *
  CAA AAA TTC AAG GGA CGC GTC ACA TTG ACT GTA GAC ATT TCC GCT AGC
  Q   K   F   K   G   R   V   T   L   T   V   D   I   S   A   S>

      300     310     320     330
    *   *   *   *
  ACA GCC TAC ATG GAG CTC AGC AGC CTG AGA TCT GAG GAC ACT GCG GTC
  T   A   Y   M   E   L   S   S   L   R   S   E   D   T   A   V>

      340     350     360     370     380
    *   *   *   *   *
  TAC TAT TGT GCA AGA GGG GGT TAC GAC GGA TGG GAC TAT GCT ATT GAC
  Y   Y   C   A   R   G   G   Y   D   G   W   D   Y   A   I   D>

      390     400     410     420     430
    *   *   *   *   *
  TAC TGG GGT CAA GGC ACC CTG GTC ACC GTC TCC TCA GCC TCC ACC AAG
  Y   W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K>

      440     450     460     470     480
    *   *   *   *   *
  GGC CCA TCG GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG
  G   P   F   S   P   L   A   P   S   S   K   S   T   S   G>

      490     500     510     520
    *   *   *   *
  GGC ACA GCG GCC CTG GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG
  G   T   A   A   L   G   C   L   V   K   D   Y   F   P   E   P>

      530     540
    *   *
  GTG ACG GTG TCG
  V   T   V   S>
  
```

FIG. 11



App No.: 08/700,737
Title: "Humanized Immunoglobulin"
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      10      20      30      40
ATG * AAG TTG CCT GTT AGG CTG TTG CTG TTC TGG ATT CCT
M K L P V R L L V L L L F W I P>
      50      60      70      80      90
BSDE I
GTT TCC GGA GGT GAT GTT GTG ATG ACT CAA AGT CCA CTC TCC CTG CCT
V S G G D V V M T Q S P L S L F>
      100      110      120      130      140
GTC ACC CCT GGA GAA CCA GCT TCT ATC TCT TGC AGG TCT AGT CAG AGT
V T P G E P A S I S C R S S Q S>
      150      160      170      180 Asp 718 190
CTT GCA AAG AGT TAT GGG AAC ACC TAT TTG TCT TGG TAC CTG CAG AAG
L A K S Y G N T Y L S W Y L Q K>
      200      210      220      230      240
*Msc I *
CCT GGC CAG TCT CCA CAG CTC CTC ATC TAT GGG ATT TCC AAC AGA TTT
P G Q S P Q L L I Y G I S N R F>
      250      260      270      280
TCT GGG GTG CCA GAC AGG TTC AGT GGC AGT GGT TCA GGG ACA GAT TTC
S G V P D R F S G S G S G T D F>
      290      300 NruI      310      320      330
ACA CTC AAG ATC TCG CGA GTA GAG GCT GAG GAC GTG GGA GTG TAT TAC
T L K I S R V E A E D V G V Y Y>
      340      350      360      370      380
TGC TTA CAA GGT ACA CAT CAG CCG TAC ACG TTC GGA CAG GGG ACC AAG
C L Q G T H Q P Y T F G Q G T K>
      390      400      410 Kas I
GTT GAA ATA AAA CGG GCT GAT GGG GCG CC
V E I K R A D A A P>

```

FIG. 12



LIGHT CHAIN OLIGOS:		DOUBLE STRAND FRAGMENTS
L1	5'- TTT CCG GAG GTG ATG TTG TGA TGA CTC AAA GTC CAC TCT CCC TGC CTG TCA CCC CTG GAG AAC CAG CTT CTA TCT CTT GCA GGT CTA GTC AGA G	LA
L2	5'- ACT GGC CAG GCT TCT GCA GGT ACC AAG ACA AAT AGG TGT TCC CAT AAC TCT TTG CAA GAC TCT GAC TAG ACC TGC AAG AGA TAG AAG CTG GTT C	
L3	5'- CCT GGC CAG TCT CCA CAG CTC CTC ATC TAT GGG ATT TCC AAC AGA TTT TCT GGG GTG CCA GAC AGG TTC AGT GGC AGT GGT TC	
L4	5'- ACT CGC GAG ATC TTG AGT GTG AAA TCT GTC CCT GAA CCA CTG CCA CTG AAC CTG TCT GGC ACC CCA GAA AAT CTG TTG GAA ATC	LB
L5	5'- TCT CGC GAG TAG AGG CTG AGG ACG TGG GAG TGT ATT ACT GCT TAC AAG GTA CAC ATC AGC CGT ACA C	LC
L6	5'- ATG GCG CCG CAT CAG CCC GTT TTA TTT CCA CCT TGG TCC CCT GTC CGA ACG TGT ACG GCT GAT GTG TAC CTT GTA AGC AGT AAT AC	
HEAVY CHAIN OLIGOS		DOUBLE STRAND FRAGMENT
H1	5'- ATA AGC TTC GCC ATG AAA TGC ACC TGG GTC ATT CTC TTC TTG GTA TCA ACA GCT ACA AGT GTC CAC TCC CAG GTC CAA CTA GTG CAC CGG TTA	HA
H2	5'- TAA CCG GTG CAC TAG TTG GAC CTG GGA GTG GAC ACT TGT AGC TGT TGA TAC CAA GAA GAG AAT GAC CCA GGT GCA TTT CAT GGC GAA GCT TAT	HB
H3	5'- CAA CTA GTG CAG TCT GGG GCT GAG GTT AAG AAG CCT GGG GCT TCA GTG AAG GTG TCC TGC AAG GGT TCT GGC TAC ACC TTC ACC AGC	
H4	5'- TAA CCG GTA CTC TAG ACG TTG GCC AGG CGC CTG CCT CAC CCA ATG CAT CCA GTA GCT GGT GAA GGT GTA GGC AGA ACC CTT GCA GGA C	HC
H5	5'- CGT CTA GAG TGG ATC GGA GAG AIT GAT CCT TCT GAG AGT AAT ACT AAC TAC AAT CAA AAA TTC AAG GGA CGC GTC A	
H6	5'- TAA CCG GTG TGC TAG CGG AAA TGT CTA CAG TCA ATG TGA CGC GTC CCT TGA ATT TTT GAT TGT AGT TAG TAT TAC T	HD
H7	5'- CCG CTA GCA CAG CCT ACA TGG AGC TCA GCA GCC TGA GAT CTG AGG ACA CTG CGG TCT ACT ATT GTG CAA GAG GGG GTT ACG ACG GAT G	
H8	5'- TCA CCG GTG CGG TGA CCA GGG TGC CTT GAC CCC AGT AGT CAA TAG CAT AGT CCC ATC CGT CGT AAC CCC CTC TTG CAC AAT AGT AGA C	HE
H9	5'- CTG GTC ACC GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA G	
H10	5'- TCA CCG GTT CGG GGA AGT AGT CCT TGA CCA GGC AGC CCA GGG CCG CTG TGC CCC CAG AGG TGC TCT TGG AGG AGG GTG CCA GGG G	

FIG.. 13



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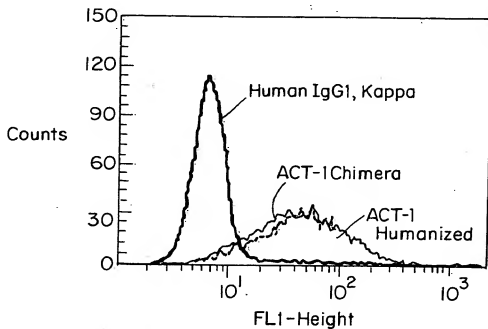


FIG. 14



App No.: 08/700,737
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Inventors: Paul D. Ponath, *et al.*

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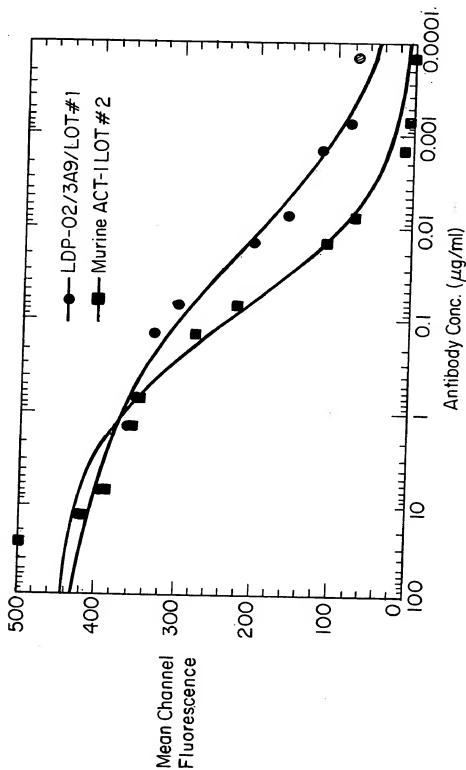


FIG 15

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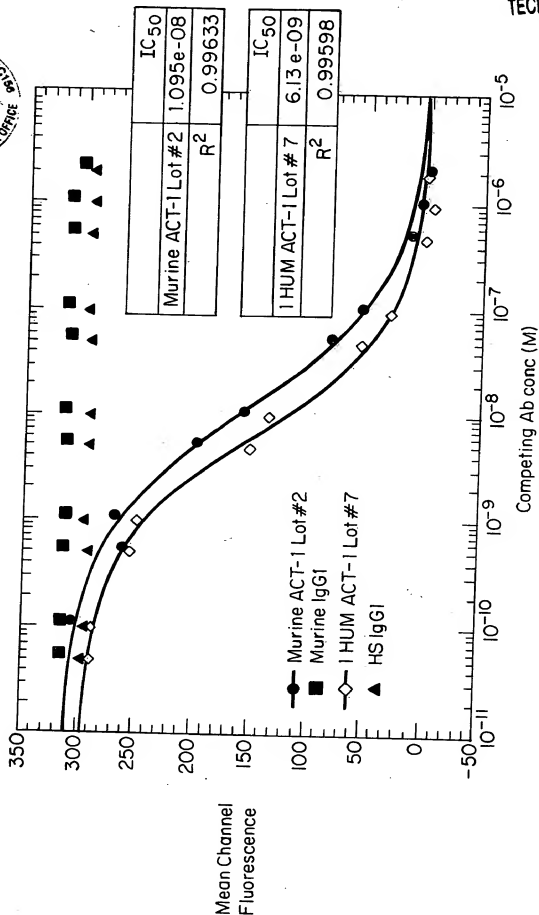


FIG. 16



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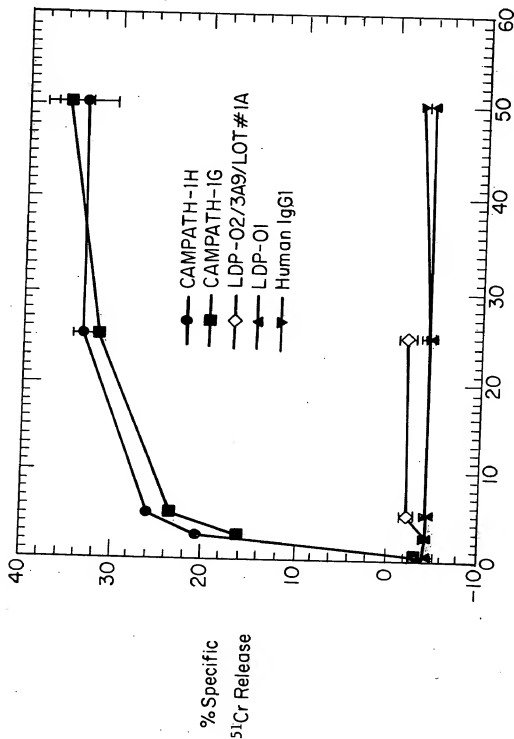


FIG. 17



App No.: 08/700,737
 Title: "Humanized Immunoglobulin ..."
 Inventors: Paul D. Ponath, *et al.*

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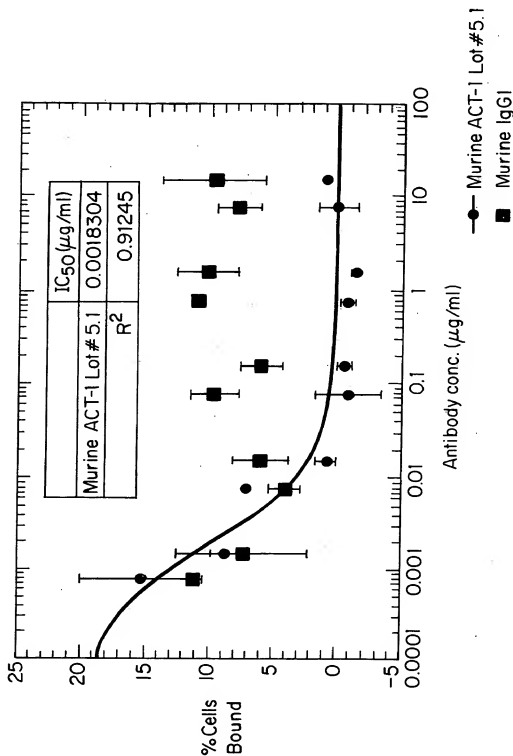


FIG. 18A



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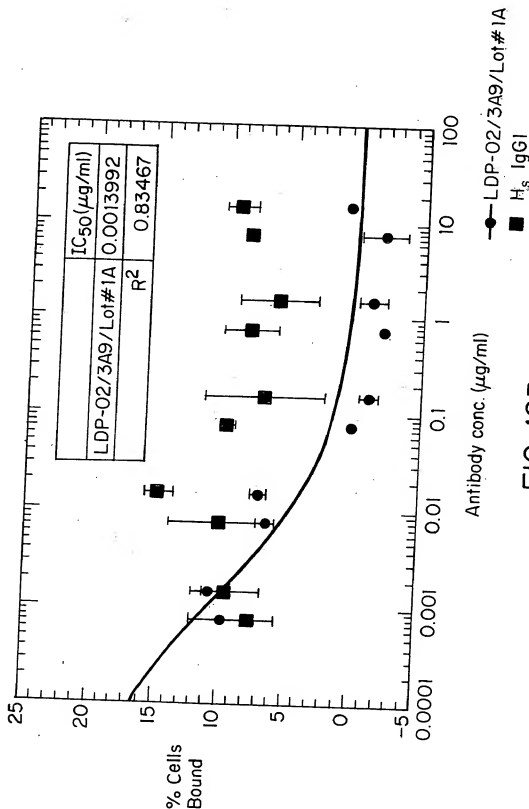


FIG. 18B



App No. 08,700,797
Title: "Humanized Immunoglobulin ..."
Inventors: Paul D. Ponath, *et al.*

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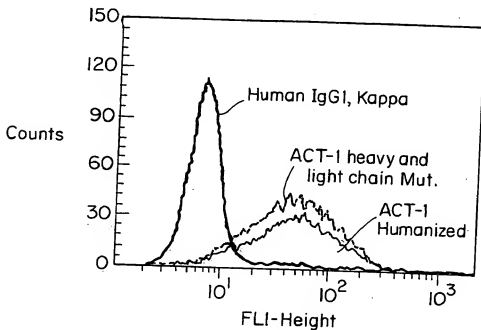


FIG. 19